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By W. M. Haffkine.

The object of the present paper is to give a brief sketch of the work which I have done in India during 1893 and 1894.

Ten years have elapsed since this city was visited by Robert Koch for the purpose of investigating the causes of cholera. The researches, which have since then been carried out in various parts of the world and under most different conditions, all tend to confirm his original results. In spite of the most careful researches, no other microbe has been found besides the *comma bacillus*, that is constantly associated with the disease, and is not to be found in any other circumstances.

Cholera, as a natural disease, is not known among animals. Even man in an average state of health exhibits a high degree of resistance to this disease, although the differences observed in this respect in a *number* of individuals are very great. In correspondence with these facts, it has been shown that animals do not become affected by the comma bacilli in a way recalling the symptoms of cholera, and that an artificial infection tried on healthy men remains in a very large proportion of cases without effect. The toxic power of the comma bacilli can, however, be shown in many ways. In the majority of domestic and other animals, when introduced into their abdominal cavity, often in minimal quantities, the comma bacilli produce a fatal effect. The same result is observed when the cholera microbe is injected into the depth of the muscular tissue. Its introduction into the circulatory system is accompanied by important disturbances of health, which may be fatal.

But the disease thus produced in animals does not present the symptoms peculiar to cholera, and when given per os, and thus introduced into the alimentary tract, the comma bacilli remain without effect.

It is easy to show that, by preventive treatment with attenuated cholera virus, the animals can be protected against all those forms of artificial infection, which otherwise would be fatal to them. Ferran in Spain, in 1885, experimenting on very young guinea-pigs, which used to succumb to a hypodermic inoculation, has shown the protection with regard to this form of infection. In 1892, Brieger, Kitasato and Wassermann, and myself have shown an immunization against peritoneal inoculation. I have demonstrated that animals can also be protected against the infection in the muscular tissue. A number of investigators have repeated these experiments with the same results, and on different species of animals.

But the chief question whether it is possible to protect man against the particular form of disease to which he is subject cannot be solved by these experiments beyond a certain degree of probability.

On the other hand, the infection of the *intestinal tract* of lower animals by the comma bacilli can be produced only under circumstances which tend to obscure the results and make the conclusions drawn from them uncertain. The usual method adopted for this kind of infection, since the experiments of Koch, consists in introduction into the stomach of a 5 per cent. solution of carbonate of soda and of the injection into the peritoneum of an alcoholic solution of opium in the proportions of one gram. of the tincture to 300 grams. of the weight of the animal. The dose of the microbe is then introduced by a sound into the stomach.

The first of these three processes, the injection of soda, is intended, by neutralizing the contents of the stomach, to prepare a free passage for the comma bacilli, which else would be killed by the gastric acids. But by this neutralization of the acids the natural disinfection of the stomach is stopped, and in a few hours this organ is found to be swarming with a multitude of microbes, which penetrate into the intestine at the same time as the comma bacillus. The consequences of this is that the ingestion of soda by itself, without the two other operations, in a large number of cases disturbs the health of the animal.

The second part of the operation, the injection of opium into the peritoneum, has for its object the stoppage of the peristaltic movements of the intestines, thus to facilitate the act of infection. This preparation is often fatal to the animal. Without the subsequent infection with the comma bacilli, animals thus treated with soda and opium succumb in a large proportion of cases.

Lastly, the third part of the procedure, the introduction of the comma bacilli, when taken *per se*, is absolutely harmless to the animal.

Thus, in this combination of three different processes which are employed to produce an imitation of cholera in animals, the last one, the process which is to be studied, is the one which has the smallest effect, and is easily obscured by the two others.

When two groups of animals, one subject to some protective treatment by cholera virus, the other not, are exposed to this combined operation, both groups are equally affected by the first two processes, and it becomes difficult to discern the difference in the action on them of the last process. The administration of opium must be done with great care, and a third control set of animals must be taken for comparison, which are treated with soda and opium alone. The difference between the protected animals and the unprotected can then be easily put in evidence. As to whether inoculation is protective under these conditions, contradictory results have been obtained. Brieger, Kitasato and Wassermann, Klemperer and myself have succeeded in obtaining animals protected against the intestinal forms of infection, whereas Pfeiffer and Wassermann, Sobernheim, Zabolotny have only obtained negative results.

The method which has been applied lately by Mons. Metchnikoff for the intestinal infection of very young rabbits, and which consists in an admixture with the comma bacillus of two other microbes, has not got over the difficulty. The two auxiliary microbes are supposed to increase the effect of the comma bacillus; but this in its turn reacts on the two microbes. Both groups being equally harmless by themselves, it is impossible to decide whether illness or death of the animal is produced by the comma bacilli, or by the two other microbes.

The laboratory experiments on men are attended with still greater difficulties. Judging by the observation hitherto made on cholera, it is to be expected that, if an attempt had been made on a hundred men to infect them with cholera by ordinary cholera vibrios, not more than five, or, ten, or, in the most favourable conditions, twenty of them would show symptoms of the disease, and in about half of this number the experiment would prove fatal.

Attempts have, however, been made in Germany, France and Austria to facilitate the experiment on man by producing artificial gastric disorder preliminary to the infection by comma bacilli. I need not say that these attempts have been made by the investigators first of all on their own persons and afterwards on people who offered themselves voluntarily and with full knowledge of the danger they were undergoing. The result showed great individual differences in regard to the susceptibility to the disorders produced by the preliminary operations and by the infection. A disease, though mild, resembling in all main features cholera, has been produced in only one case, which occurred in the group of experiments carried out by Mons. Metchnikoff. In a certain proportion of cases the experiment resulted in a more or less persistent attack of diarrhœa, and others remained unaffected.

At this rate, for producing in the laboratory ten or twenty cases of cholera, in order to try on them any preventive or curative treatment a trial must be made at an infection of two or three hundred individuals, with a strong infective virus.

The method which I adopted was to attempt not to infect, but to save, during an epidemic or on the approach of such a certain number of individuals, basing my actions on the exact knowledge which could be obtained from laboratory experience; and by comparing the fate of the treated individuals with that of the non-treated, to draw the final conclusion as to the effect of the treatment.

An attempt of a similar kind has been already made in Spain during the epidemic of 1885, by Dr. Ferran. As has previously been mentioned, this observer noticed that young guinea pigs, inoculated under the skin with a certain dose of cholera virus, succumbed, whereas when previously injected with smaller and tolerated doses, they became able to stand otherwise fatal hypodermic injections. He accordingly made cultures of cholera microbes in liquid medium, and applied these for injections in man.

The results of these operations were never clearly ascertained. The account of Dr. Shakespeare, the American investigator, is highly commendatory as to the effect of the treatment. The delegates of the French, Russian and some other European Governments returned back bringing with them unfavourable accounts. A study of the numerous data, published by Ferran since, failed to produce conviction in the efficacy of the treatment employed by him, and the whole question remained open.

In Ferran's procedure must be recognized a source of uncertainty, which tended, first, to vitiate the results; and secondly, to render the method inapplicable as a general measure. This source of uncertainty was the employment for purposes of treatment of a virus taken directly from a diseased subject. Microbial virus in nature is extremely variable in its properties and in its pathogenic strength. This rule is especially applicable to those forms of virus, which are capable of growing outside the animal body, and, in a still higher degree, which, like the present, are incapable of protecting themselves by the formation of spores. A comma bacillus may be fatal to a guinea-pig when injected into the peritoneum in the dose of one hundredth of a culture, while another will be harmless when used in a dose five hundred times larger than this. Whereas the ordinary comma bacillus is without effect when injected under the skin of an adult guinea-pig, others are to be met with which will kill under these conditions when used in minimal doses. The comma bacillus, as a rule, is without effect on pigeons (and on birds generally); but, during the epidemic in Massouah in 1890 and during the last years in Europe, several specimens have been isolated, fatal to these birds. On the other hand, one and the same specimen, when cultivated in the laboratory for any length of time, undergoes considerable alterations in its power. Mons. Metchnikoff quotes the example of a comma bacillus isolated in France, which gradually diminished in power to about one 75th of its primitive strength. It is evident, therefore, that a virus, taken from a diseased organism, varies from being a very dangerous one to one which will be without any effect on the most susceptible individual.

The use of virus of such origin for purposes of treatment has now been finally condemned in the case of small-pox. The discovery of a method of cultivating and keeping of a lymph of a well determined degree of virulence constitutes the work done by Jenner at the end of the last century. The researches of Pasteur have elucidated the principles of the transformation of virus, and a problem similar to that of Jenner has been solved by him in regard to three diseases of animals (chicken-cholera, anthrax and pig-measles) and one disease common to animals and man, namely, hydrophobia.

To Gamaleia belongs the credit of having made the first attempt to find out a means of fixing the strength of the cholera virus. The method which he applied was based on the procedure employed by Koch for producing intestinal infection in guinea-pigs, with the help of carbonate of soda and of opium. The inadequacy of this method depends on the fact, that the intestinal canal is populated by a flora and fauna of other organisms, and on the impossibility of breeding there a virus in a pure culture. The result of the introduction of a virus into a medium, occupied by other microbes, depends on the nature of the latter, and since the microbial population in the stomach and intestines of animals is constantly varying, a regular cultivation of the comma bacillus in the digestive tract for the purposes of a regular modification of its qualities is impossible.

The method that I worked out for transforming the cholera virus into a vaccine of a fixed nature is based on the cultivation of the cholera bacilli in the peritoneal cavity of guinea-pigs. The rules which it is necessary to observe in order to obtain an uninterrupted series of passa ges, from animal to animal, the modification gradually produced in the virus by these procedures, the attenuation of this vaccine in order to deprive it of its necrotising properties, and to transform it into a mild first vaccine, have been described originally in the "Comptes Rendus des Séances de la Société de Biologie de Paris," and in different English Medical Journals, and need not be referred to here. It suffices to say that the two modified races of cholera virus, which I obtained, have put in our hands a means of protecting animals with certainty, and in an absolutely safe manner, against all forms of infection by the cholera virus, fatal to them; and the problem then had to be approached of putting to the test these vaccines, the harmlessness of which for man has been proved first of all on myself and on all people connected with my laboratory.

Cholera has visited Europe several times since the year 1832, and on each visit has produced great ravages in the populations of the West; but it is not a disease endemic in that part of the world, and it reappears there only after very long intervals. It was in the home of cholera, in the delta of the Ganges, that a trial of preventive inoculations for that disease had to be made.

For those who, in Europe or in any other places, will judge my work from the point of view of a laboratory research, and will discuss the most convenient conditions for getting precise answers to theoretical questions, I must say from the beginning that I was not and am not master of the plan of my operations. A country and a free population, and the various influences and currents of opinions intervening, and religious feelings and traditions, and the mixture of confidence and distrust on the part of individuals and communities are conditions differing from that in which a quietly elaborated plan of operations is put to test in the walls of a laboratory or on an experimental field of cultivation, or in other similar conditions.

The first problem, which I had to solve, was to find out whether the inoculations generally could be applied in India, and whether it was possible to induce masses of inhabitants to undergo the treatment in large bodies of people, as it was necessary for my work. Those who know the East and the conditions in the eastern populations, and who have been present at my first efforts, do not require to be reminded on the difficulties which attended this task. It is clear that the choice of best conditions, or of any conditions whatever, was out of question for me. It required a year's persistent work, and inoculation of many thousands of volunteers in distant points of the N.-W. P. and Oudh and of the Punjab, in all classes of population, before I became able to direct my work to such points of the country and to such classes, where the conditions answered the scientific requirements of the problem.

I could not carry with me a laboratory. It was most fortunate for my work that a short time before my arrival in India the Government of the N.-W. P. and Oudh decided to found a bacteriological establishment in that part of the country and entrusted it to the able direction of Professor E. H. Hankin. He and his laboratory were of the greatest help to me during the whole time of my work in the upper part of India. But great as was this assistance, it was far from being sufficient. I mentioned already the great variations which the cholera virus undergoes when cultivated in the laboratory. For keeping it at the required state, it is necessary to pass it constantly through animals, in the same way as a vaccine lymph must be always taken fresh from a calf or a child, if one wants to have it at its full power. It is sufficient to say that, when I came from Calcutta to Agra for the first time, I was able to procure and to bring with me only six of the required animals. The most essential part of my method, which forms its distinguishing feature, could be carried out, during the whole time of my nomadic operations in the country in a most unsatisfactory manner.

It must not be forgotten that, from the commencement, I announced that the protection which I hoped to obtain was not yet established as certain, and the operations, which I was about to perform, constituted an attempt or trial in that direction. I could only offer the possibility of protection and an assurance of harmlessness, an offer which could not be a great inducement for many to subject themselves to discomfort and temporary illness and loss of time connected with the operation. Before the first observations have been made in a cholera place and the fear of the operation dissipated, I was obliged to content myself with inoculations producing only slight effect, a low degree of fever, and which in many cases left the subjects without any marked reaction at all. In the experimental inocualtions which had been done in Europe, in France and England, a dose of $\frac{1}{8}$ of a culture tube has been used for each adult person. In the first inoculations in Agra I reduced the dose to only $\frac{2}{3}$ of that amount, *i.e.*, to $\frac{1}{12}$ of a tube. Two accidents, which in themselves had nothing to do with the operation, attended the first inoculations, and the whole operation being unknown to the public and easily impressing the minds, I had to reduce the dose further to $\frac{1}{20}$ of a tube. The necessity of using weak doses has been still more impressed on me when I arrived at Delhi, where I could start the inoculations exclusively on condition of using reduced doses of vaccines.

The agreement of the people and their consent to undergo a new and unknown operation were the only circumstances which guided me in the determination of the doses. In the absence of any information on the adequacy or inadequacy of these doses, and in the necessity to conform to circumstances, or to abandon my problem altogether, without any prospect of its being done in better circumstances, I chose finally the first alternative.

The inoculations have been done in the following order: in Agra, Aligarh, Jhansi, Lucknow, Sanawar, Kasauli, Dagshai, Delhi, Patiala, Simla (and Jutogh), Rajpurah, Sangrur, Rawal Pindi, Murree, Peshawar, Chirat, Nowshera, Naini Tal, Almora, Ranikhet, Dworahat, Kainur, Sakniana, Musagali, Paori, Srinagur, Tehri, Mussooree, Dehra Dun, Hardwar, and Jawalapur, Saharanpur, Lahore, Mean Meer, Sialkot, and Sansi Village, Pasrur, Searenwali, Amritsar, Kapurthala, Wazirabad, Dharmsala and Gujerat. In some other places inoculations have been done by those who studied the necessary *technique*.

The number of individuals inoculated upcountry was 22,603; of these 8,473 have been done in the N.-W. P. and Oudh, and 14,130 in the Punjab. With the 9,563 inoculated since then in Bengal, Behar and Assam, the total number of inoculated up to now is 32,166. The town where the largest number have been inoculated was Patiala. About two-thirds of the total number have been reinoculated with the second vaccine from five days to two months after the first, bringing thus the number of performed operations to a little below 50,000.

Of each man inoculated a record has been kept giving the name, age, sex, religion and caste, birthplace, profession, address, remarks on health and previous attacks of cholera, the date of first inoculation and the date and dose of second inoculation. In case of soldiers the fact of inoculation has been entered in the medical history sheet; in case of people in prison, in their jail ticket. The Principals of schools kept a list of the inoculated children (the inoculation, in case of minors, have always been done exclusively with the consent or desire of their guardians). Many Civil Surgeons preserved in their offices a record of the inoculated civil inhabitants; to others such a record will be sent. In this manner observations have been made possible in the future in different parts of the country at the time of cholera outbreaks.

During the year of 1893 two outbreaks of cholera, both insignificant, came to my knowledge in Upper India, where I was working. One was in villages near Saharanpur, another in villages near Gujranwalah. Immediately after having heard of these outbreaks the local authorities have been asked whether it will be possible to apply the inoculations in the affected places. On both occasions the answer was a negative one. Towards the end of 1893 another attempt was made through the authorities in a station of the E. B. S. R., which had been attacked by cholera. The answer this time was negative also. On different occasions, when large numbers of people had been already inoculated in different places, I made enquiries in Calcutta, whether inoculations could be applied there, but the result was invariably negative, and it was believed that the people here, being more educated but also more timid than in other parts of India, the difficulties for my operations would be particularly great. In the beginning of 1894, Surgeon-Major Lewtas, then Civil Surgeon in Chittagong, wrote to me in Amritsar, saying that a certain number of Europeans in his station expressed the desire to be inoculated against cholera, and asked me to send him vaccines, the use of which he had learned during my operations in Simla. As Chittagong lies in the endemic area of cholera, I availed myself of the opportunity of asking Dr. Lewtas to help me to introduce the inoculations in a large scale in that town. Dr. Lewtas did everything in his power to prepare for me this result. I started for Chittagong immediately.

But in my passage through Calcutta a small outbreak of cholera occurred round a tank, in a suburb of that city. Dr. W. J. Simpson, the Health Officer, asked me to investigate with him the water of that tank and to arrange experiments for the detection of the cholera microbes. Cholera microbes, indeed, were detected in this water, and at the same time we discovered the possibility of applying the inoculations in the affected huts of the bustee, at the height of the cholera season. On the 11th of March 1894, preventive inoculations were done for the first time in India in a place where cholera existed, one year and six days after I landed in this country. In the course of about a month, with the aid of that excellent arrangement of Indian Medical Inspectors of the Health Office of Calcutta, we had about a thousand people inoculated in the most affected parts of the metropolis, and the first observations were not long in forthcoming.

The question which has always been most difficult to answer was, how I could collect my observations, and, when collected, what possible conclusion could be drawn from them. In a city like Calcutta, with over 800,000 inhabitants, was I to inoculate half of the population for the purpose of comparing inoculated with non-inoculated and of testing my method ?

For a long time in different parts of India I was asked this question with an air of absolute scepticism. It was, indeed, impossible for me to inoculate whole cities. Besides the intellectual part of the populatien almost does not suffer from cholera at all, and the part which chiefly suffers from it is exclusively composed of classes whose fate cannot be traced afterwards, who move constantly from place to place and are soon lost sight of. Outbreaks among the troops or in jails are, indeed, very rare. In all Bengal and Madras Central Jails during the last 10 years, the mortality from cholera was practically *nil.* It is impossible to know even with an approximate degree of probability the part of the country where any considerable outbreak might occur, and at the time when cholera does break out, it is useless to attempt to get to the place, for applying any preventive method, cholera making its ravages very rapidly and disappearing as suddenly as it appeared.

I must confess that this unanimous verdict on my proposed work made on me a deeply painful impression. I must say that when I undertook this work, I had not an adequate idea of the difficulties which were in store for me, great as were those which I was ready to face.

I was mistaken, while in Europe, as regard the facts relating to the distribution of cholera in India. And those who were more familiar than I was with the conditions of this country, it is strange to say, did not notice for a moment my mistake. I thought it possible to select in India a village or a small town, of three or four thousand inhabitants, which suffer regularly from a well-known amount of cholera ; by inoculating, before the cholera season, a half or a large portion of this single village, in this way a field would be prepared for observing, in the course of one year, two epidemics of cholera, of perhaps a couple of hundred cases each, and for judging of the effect of my operation. How different were the difficulties connected with such a project, from those which actually awaited me !

The problem was solved in a way which revealed itself only after a long period of work. It was not necessary to inoculate half a country, or a city, or even half a village. In the endemic area each house can comprise within its wall an experimental group. By inoculating a certain number of these houses, selected in affected quarters, there is the probability of cholera appearing in some of them and allowing of comparisons between the inoculated and not inoculated members of the house, who otherwise are under similar conditions of food, water, soil, social customs, &c.

As regards inoculations in areas where cholera did not exist, where I had to work during my first year of operation, I had to decide upon spreading the inoculation in as many localities and regiments as possible, leaving to epidemiological laws, the selection of locality where the result of my work could be later on observed. The first method gave results in Calcutta, the second in Lucknow and Cawnpore.

A third method was adopted in Gaya Jail where, on the appearance of an outbreak, measures were taken to apply the preventive treatment at once and to take advantage of the later part of the epidemic.

In Calcutta inoculations have been carried out from the beginning of March of this year till the present time; 3,478 persons have submitted themselves to inoculation. In 13 houses cholera appeared from 2 to 180 days after the inoculations have been carried out. The total number of the inhabitants of these houses was 181. Out of this number 85 were inoculated, 96 untreated. The number of cases of cholera that occurred among the 85 inoculated is 1, which was followed by a fatal issue, giving a percentage of attacks and deaths of 1·18 per cent. The number of attacks among the 96 non-inoculated was 15, and of deaths 11, giving a percentage of cases 15·63 per cent., and of deaths total 11·63 per cent. The case of a child in a cholera bustee who was suffering from diarrhœa at the time of inoculation and developed typical cholera within an hour of the treatment is not included in the above statistics.

Of soldiers who had been inoculated by Mr. Hankin in Cawnpore, thirteen months previously, 75 were present on the occasion of the epidemic of last August, and were located in barracks with 177 non-inoculated. During the epidemic 19 cases of cholera and 13 deaths occurred among the non-inoculated. No cases occurred among those who had been treated.

In Gaya Jail I arrived on the 18th July of this year, at a time when cholera had already broken out, and six cases and five deaths had occurred. During the epidemic which lasted a fortnight longer, on an average 409 were present. Of these 207 were inoculated, and 202 remained without treatment. Among the non-inoculated 20 cases of cholera appeared with 10 deaths. The inoculated presented 8 cases, and of these 5 led to a fatal issue. The distribution of cases among both groups is to be seen in detail in the following table :—

During the first five days after inoculation :—

Not inoculated	...	7 cases	with 5 deaths.
Inoculated	...	5 „	4 „

During the next three days :—

Not inoculated	...	5 cases	3 deaths.
Inoculated	...	3 „	1 death.

The last six days :—

Not inoculated	...	8 cases	2 deaths.
Inoculated	...	*Nil*	*Nil*

It will be observed from this table that the difference in figures increased gradually until the eighth day. This difference was *nil* on the first days after the inoculations were carried out; and it is seen to have increased gradually till the eighth day after the first day of treatment. A similar phenomenon has been observed in vaccination against small-pox.

I am of opinion that in a milder epidemic the protective influence would show itself in a more marked manner also in the first few days after inoculation. I base this opinion on the well ascertained results of laboratory experiment.

Whereas in Gaya the treatment was applied during the epidemic, in Lucknow the epidemic occurred 14 to 15 months after the inoculations. The results were as follows:—

	Cases.	Deaths.
640 Non-inoculated	120	79
133 Inoculated	18	13
	Pc. of cases to strength.	Pc. of deaths to strength.
Non-inoculated	18·75 per cent.	12·34 per cent.
Inoculated	13·53 ,,	9·77 ,,

With regard to all these results three possible points of view can be taken up.

Firstly, that the fact of the protection of animals against all forms of the cholera virus is of no significance whatever; that the Calcutta results are a mere coincidence; those in Gaya also a coincidence; the differences in the occurrences among the inoculated and non-inoculated in Lucknow are equally accidental, and only those who died in the latter locality can be quoted as bearing on the subject and completely condemning the method.

Secondly, another point of view is that the fact of the immunization of animals proves that a living organism is capable of being protected against the cholera virus; that the Calcutta results are quite comprehensible in this light; that the Gaya results are of a similar nature; that the difference in the fates of the inoculated and non-inoculated in Lucknow is also an illustration of the above law, and that the cases of failure are due to the lapse of time and the vanishing of the effect of inoculation, which could not be determined beforehand.

Thirdly, the following view may be held: The first four facts are proofs of the value of the inoculation, and the cases of failure in Lucknow are due to both the lapse of time that occurred since the carrying out of the inoculations, and the feeble reaction produced on the subjects on the time of the treatment. Indeed, as is recorded in the Lucknow registers, out of the 185 men inoculated in the East Lancashire Regiment 66 showed no fever after the inoculation, 70 had only a sight rise of temperature, and in only two out of the whole number was the febrile reaction well marked. (This result was due to the mildnes of the virus employed and the relatively small doses in which it was injected.) It is a well-established law that the amount of protection conferred, whether in small-pox, anthrax or any other disease, is in direct relation to the amount of fever produced at time of the inoculation.

The number of observations is not sufficient and the time is not ripe for discussion, nor for an attempt to bring about a general consensus of opinions. I intend to do everything in my power in order to obtain facts or deciding definitely between these three possibilities, a decision which, in my opinion, can only be brought about by an increased number of observations, and not by discussion.

I will point out, however, one fact, namely, that the harmlessness of the operations, whether in the presence or absence of cholera, is now definitely established. This is proved by the examination of the figures. Summarising the occurrences among the inoculated and uninoculated, and disregarding the question whether they were accidental or not, we have the following results:—Total number of those on whom observations have been made in Calcutta, Gaya, Cawnpore and Lucknow is 2,235. Of these were inoculated 500 and 1,735 not inoculated.

Inoculated had 21 attacks and 19 died, giving a percentage of cases to total of 4·2 and deaths to total 3·8 per cent.

Uninoculated had 174 attacks and 113 died, giving a percentage of cases to total of 10·63 per cent. and deaths to total of 6·51 per cent.

These figures not only show that the inoculations are harmless, but show a difference in the occurrences that, if interpreted, can only be interpreted in favour of the inoculations.

In conclusion, I beg to express my thanks to all those who have so kindly helped me in carrying out this work. I appeal to Medical Officers and to others to give me further facilities for bringing a conclusion to this important question, by helping me in collecting observations and in spreading the inoculations in the most appropriated places for this.